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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
| 10/749,120 | 12/30/2003 | Richard Boyd | NOR-015CP2 and 286336.154 | 3284 |
| 23483 | 7590 | 08/15/2008 | EXAMINER | |
| WILMERHALE/BOSTON 60 STATE STREET BOSTON, MA 02109 | | | SAUNDERS, DAVID A | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1644 | |
| | | | NOTIFICATION DATE | DELIVERY MODE |
| | | | 08/15/2008 | ELECTRONIC |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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|------------------------------|--------------------------------------|------------------------------------|--|
| Office Action Summary | Application No. 10/749,120 | Applicant(s) BOYD ET AL. | |
| | Examiner David A. Saunders | Art Unit 1644 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 5/30/08.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38-44, 46-57, 61-64, 66-84, 89, 90, 92 and 94-100 is/are pending in the application.
- 4a) Of the above claim(s) 43, 61-64, 66-84, 90, 92 and 94-98 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38-42, 44, 46-57, 89, 99 and 100 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/30/08 has been entered.

Claims 38-44,46-57,61-64,66-84,89-90,92,94-100 are pending. Claims 38-42,44,46-57,89,99-100 are under examination.

OBJECTION(S)/REJECTION(S) OF RECORD WITHDRAWN

The amendment has overcome previously stated issues as follows:

The objection to claim 45 under 37 CFR 1.75, due to its cancellation.

MAINTAINED REJECTION(S) UNDER 35 USC 112, FIRST PARAGRAPH

Claims 38-42,44,46-57,89 and 99-100 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 38 and 58 recite new matter.

In, the amendment filed 11/16/07 applicant has urged that the recitation of "markers" at page 58, lines 1-3 and the recitation of "markers" at page 64, line 10-15 provide support for the now claimed combination method, in which both a blood/serum marker of thymus activation, and newly produced T-cells are monitored by TREC analysis. Applicant has argued again, in the response filed on 5/30/08, that the recitation of the phrase "following the concentration of one or any combination of these markers, one can monitor activation of the thymus", at page 58, lines 1-3, should be considered to encompass not only those markers recited in section A, in which this phrase appears but, also, to those markers in sections B and C, which follow on pages

63 and 64. With respect to the “Newly Identified Markers” of section B, no consideration is necessary since TRECs are certainly not “Newly Identified”.

In the previous action, the examiner noted that all of the “markers” of section A are blood or serum markers. Applicant’s arguments of 5/30/08 have urged that TRECs are also within the scope of blood or serum markers, since the T-cells are isolated from whole blood. This argument is not convincing for the following reasons:

The examiner presently elaborates upon the literal reasons as to why the “markers” of section A cannot be considered as also encompassing the markers of section C. More particularly, the teachings that refer to “any combination of these markers” in section A must be taken in full context. The full teachings at p 58, lines 1-3 are that “by following the concentration of one or any combination of these markers, one can monitor activation of the thymus.” What therein do “these markers” refer to? In context, “these markers” can only refer to the markers recited in the previous sentence, which have been disclosed as “markers associated with the activation of the thymus”. Page 58, lines 1-3 are thus referring to markers of thymus activation, rather than to the markers of T-cell production taught in section C.

The examiner presently further elaborates upon the nature of the “markers associated with the activation of the thymus” in section A. One of these, IL-7 is “produced by thymic and bone marrow stromal cells”. Likewise, applicant describes FTS or thymulin as a “nonapeptide hormone as being secreted exclusively by the thymic subcapsular and medullary cells”. In other words, every “marker” described in section A is one that is reflective of the activity of thymic cells which are other than T-lymphocytes and their more immature precursors.

On the other hand, in section C, the “markers” listed as Ki67, CD69, etc. have been previously described particularly as those for the “detection of new and/or proliferating cells”. It can even be questioned whether this listing of such markers can be properly considered as encompassing “TREC analysis” since this option of “TREC analysis” is set off from the listing of as Ki67, CD69, etc by the phrase “as well as”. In any case, everything described in section C, whether it comes within the rubric of a “marker” or not, is associated with newly produced T-cells per se, as opposed to the

“markers” described in section A, which are associated with the thymic environment from which the T-cells emigrated. For these reasons, the examiner will not grant that the statement at page 58, lines 1-3 that by “following the concentration of one or any combination of these markers, one can monitor activation of the thymus” can in any way be considered as encompassing, also, the “markers” of section C.

Applicant has also urged that the examiner was in error by arguing, in the action mailed 2/21/08, that the markers of section A and of section C were not “functional equivalents”. The examiner concurs that every marker analyzed in a multi-step method of an assay claim does not need to be a functional equivalent of the others. The examiner, however, did make this statement to emphasize that the markers of section A and of section C were not “functional equivalents” in that they do not measure the same biological activity. As elaborated in an above para., every “marker” described in section C is associated with newly produced T-cells per se, while the “markers” described in section A are associated with the thymic environment from which the T-cells emigrated.

Applicant has also urged that original claim 38 supports by reciting the phrase “monitoring the level in the patient’s blood or serum one or more markers associated with activation of the thymus”. For the reasons stated further supra with respect to the teachings of page 58, lines 1-3, this phrase refers precisely to “markers” that are reflective of the activity of thymic cells, rather than to the T-lymphocytes which have emigrated from the thymus.

Finally applicant has urged that the examiner is incorrect in urging that there should have been an example in which both a blood or serum marker associated with the activation of the thymus is measured and TREC analysis is conducted. The examiner concurs that no working example is required. However, what is required is a precise indication in the disclosure that both a blood or serum marker would be measured and TREC analysis would be conducted upon a sample(s) collected from one patient at one time point. This applicant has never done. Since applicant did not do so, the Office maintains that applicant has created new matter by attempting to tie together divergent aspects of the application.

NEW REJECTION(S) UNDER 35 USC 112, SECOND PARAGRAPH

Claims 46-49 Are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 46 depends from cancelled claim 45.

NEW REJECTION(S) UNDER 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 46-47, 57 And 100 are rejected under 35 U.S.C. 102(b) as being anticipated by Boyd et al (US 2002/0136704, cited on Form PTO-892) .

This reference is cited under 102 (b) since it has a publication date more than 1 year prior to the instant filing date of 12/30/03. This reference corresponds to earlier filed application 09/977,074, for which applicant claims benefit of its earlier filing date.

The disclosure therein pertaining to the measurement of a blood or serum marker and to TREC analysis supports instant claim 38 as much as does the instant disclosure (which is no support under 112); thus for the purposes of prior art considerations, instant claim 38 is not rejected. The disclosure therein pertaining to the pharmaceuticals

administered, however, cannot support instant dependent claims 46-47 and 100. For example, at the least, "SERMs, SARMs, SPRMs" are not supported in instant claim 46. For example, at the least, "DECAPEPTYLY" and "Gonadorelin" are not supported in instant claim 47. The recitation of "ketoconazole" is not supported in instant claim 100.

The disclosure of US 2002/0136704 pertaining to the markers measured cannot support instant dependent claim 57. For example, at the least, "CXCL12, CXCL19" are not supported in instant claim 57.

The number of pharmaceuticals/markers recited in each of claims 46-47 and 57 is excessively long for the examiner to search each Markush group member. In order to overcome the rejection, Applicant must cancel all Markush members in the instant claims which lack support in the earlier documents. See MPEP201.11.

Claims 46-47, 57 And 100 are rejected under 35 U.S.C. 102(a) or (e) as being anticipated by Boyd et al (US 2003/0017153, cited on Form PTO-892) .

This reference is cited under 102 (a) since it has a publication date less than 1 year prior to the instant filing date of 12/30/03. This reference is cited under both 102 (a) and (e) since it has a different inventive entity from that instantly. This reference corresponds to earlier filed application 09/885,268, for which applicant claims benefit of its earlier filing date.

The disclosure therein pertaining to the pharmaceuticals administered cannot support instant dependent claims 46-47 and 100. The disclosure therein of the markers measured cannot support instant dependent claim 57. The rationale follows that set forth supra with respect to reference US 2002/0136704.

CONTACTS

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara, can be reached on 571-272-0878. The fax phone number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 8/12/08 DAS

/David A Saunders/

Primary Examiner, Art Unit 1644